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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/820,618	04/07/2004	Yadong Huang	GLAD-217CON	8516
24353 7590 02/20/2009 BOZICEVIC, FIELD & FRANCIS LLP 1900 UNIVERSITY AVENUE SUITE 200 EAST PALO ALTO, CA 94303				
EXAMINER				
PAK, MICHAEL D				
ART UNIT		PAPER NUMBER		
1646				
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02/20/2009		PAPER		

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/820,618

Applicant(s)

HUANG ET AL.

Examiner

Michael Pak

Art Unit

1646

Period for Reply -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06 November 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 7-20, 25-30 and 32-37 is/are pending in the application.
- 4a) Of the above claim(s) 7-11, 17-20, 25-30 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 12-16 and 32-37 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

Response to Amendment

1. Amendment filed November 6, 2008 has been entered.
2. Claims 1-6, 21-24 and 31 have been cancelled. Claims 7-11, 17-20 and 25-30 are withdrawn. Claims 12-16 and 32-37 are examined.
3. This application contains claims 7-11, 17-20 and 25-30 drawn to an invention nonelected with traverse in the reply filed on May 22, 2008. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 12-16 and 32-37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims recite or encompass the term "amino acids 244-260 of apoE" which is ambiguous and unclear because the metes and bounds of the term is not clear. The term "apoE" encompass variants and fragments and it is not clear what amino acid

position encompass if the structure can vary. Thus the amino acid positions are relative term which is ambiguous.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 12-16 and 32-37 are rejected under 35 U.S.C. 102(b) as being anticipated by Crutcher and Harmony (WO 98/01101; *15 January 1998*).

WO 98/01101 discloses a method of inhibiting the formation of neurotoxic apoE4 fragments in primary chick sympathetic neurons via protease inhibitors. WO 98/01101 teaches the use of antipain, a general serine protease inhibitor, to prevent the generation of toxic apoE4 fragments (pp. 15 Example 5). Furthermore, WO 98/01101 claims a method of treating conditions associated with apoE toxicity, including Alzheimer's disease, comprising administering a protease inhibitor, including antipain, to interfere with the production of neurotoxic fragments of apoE4. While WO 98/01101 is silent with respect to neurofibrillary tangles in a neuronal cell in an individual with Alzheimer's disease, the specification discloses that reducing the amount of apoE4 tangles will have this effect. Thus the effect on Alzheimer's disease is inherent to the method of WO 98/01101.

It is noted that the term "amino acids 244-260 of apoE" is a relative term and that Crutcher teaches the region.

Applicants argue that Crutcher and Harmony do not disclose a neurotoxic region because of the contradiction by the applicant's specification. However, as stated by applicant's argument, on page 10, Tolar uses a peptide with tandem repeat and thus cannot rule out the neurotoxic effect observed by Crutcher.

6. Claim 6-12 and 32-37 is rejected under 35 U.S.C. 102(b) as being anticipated by Tolar et al. (The Journal of Neuroscience **19(16)**: 7100-7110).

Tolar et al. discloses a method of using a protease inhibitor cocktail to attenuate the production of neurotoxic apoE4 fragments in dissociated chick, sympathetic neurons (pp. 7102 "Protease inhibitors reduced the production of truncated apoE and attenuate Neurotoxicity of full-length apoE"; Figure 1). Tolar et al. uses a protein cocktail which includes antipain, a known serine protease inhibitor. While Tolar et al. is silent on reducing the activation of an enzyme that catalyzes the formation of carboxyl-terminal truncated apoE by $A\beta_{1-42}$, the specification demonstrates that said enzyme is susceptible to inhibition by serine protease inhibitors. Thus the effect on Alzheimer's disease is inherent to the method of Tolar et al. Furthermore, Tolar et al. discloses that the protease inhibition reduces the formation of neurotoxic apoE fragments thus meeting the limitations of claim 31 (Figure 1, lower panel, western blot).

It is noted that the term "amino acids 244-260 of apoE" is a relative term and that Crutcher teaches the region.

Applicants argue that Crutcher and Harmony do not disclose a neurotoxic region because of the contradiction by the applicant's specification. However, as stated by applicant's argument, on page 10, Tolar uses a peptide with tandem repeat and thus cannot rule out the neurotoxic effect observed by Crutcher.

7. No claims allowed.

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Art Unit: 1646

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Pak whose telephone number is 571-272-0879. The examiner can normally be reached on 8:00 - 2:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol can be reached on 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael Pak/
Primary Examiner, Art Unit 1646
February 16, 2009